UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,938	10/31/2001	Salvatore Albani	UCSD1360-1	8878

7590 12/13/2006

LISA A. HAILE PH.D.
GRAY CARY WARE & FREIDENRICH LLP
4365 EXECTIVE DRIVE
SUITE 1100
SAN DIEGO, CA 92121-2133

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,938	ALBANI ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-59 and 62-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *57,59,62,63 and 66* is/are allowed.

6)☒ Claim(s) *58,64 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received September 27, 2006 are acknowledged.

Claims 1-56, 60, 61, and 67-74 have been cancelled.

Claim 59 has been amended.

Claims 57-59 and 62-66 are pending and under examination in this office action.

Specification

2. Applicant's amendments to the specification are noted and have been entered.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 64 and 65 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons of record.

The office action mailed June 28, 2006 states:

> These claims recite compositions comprising one or more peptides that consist of the recited SEQ ID numbers and a cytokine that induces a pro-inflammatory response (claim 64) or an anti-inflammatory response (claim 65). The specification teaches that the genus of recited SEQ ID numbers includes peptides that induce pro-inflammatory responses and peptides that induce anti-inflammatory responses. Pro-inflammatory peptides induce the expression of IFNγ, with an example being the peptide consisting of SEQ ID NO:4 (see particularly paragraph 100 on page 39 and Figures 15-18), while anti-inflammatory peptides induce the expression of IL-10 as exemplified by the peptide consisting of SEQ ID NO:20 (see particularly paragraph 112 on page 49 and Figure 24B). The specification indicates that the peptides and compositions of the instant invention are to be administered to subjects to induce pro- or anti-inflammatory responses, yet a composition comprising a pro-inflammatory peptide and an anti-inflammatory cytokine comprises activities that cancel each other and such a composition would not induce a pro- or anti-inflammatory response upon administration. As such the claimed products appear to lack a specific and substantial utility or a well established utility.

Applicant's arguments filed September 27, 2006 have been fully considered but they are not persuasive. Applicant argues that "the intended utility of the invention includes use of treatment regimens wherein peptides and cytokines of seemingly opposing effects

are administered" because such treatment regimens are selective manipulation of the immune response analogous to a "dimmer switch" wherein the response is tailored to the disease state.

This argument is not convincing. To support this argument, applicant points to paragraphs 9,10, and 76 stating "Paragraph 9, among others sets forth the objective of the invention, which includes administration of pro-, anti-, and mixtures of both pro- and anti-inflammatory peptides." The text of these paragraphs are provided below:

> [0009] A method of the invention can modulate an immune response by increasing or decreasing an inflammatory response associated with the immune response. Thus, in one embodiment, a method of the invention provides a means for augmenting or inducing an inflammatory response in the subject. In one aspect, the method of augmenting or inducing an inflammatory response in the subject is performed by administering a peptide having pro-inflammatory activity, i.e., a pro-inflammatory peptide, to the subject under immunizing conditions. In another aspect, the method is performed by administering an anti-inflammatory peptide to the subject under tolerizing conditions. In still another aspect of the method, a combination of immunogenic peptides is administered, for example, two or more pro-inflammatory peptides under immunizing conditions, or two or more anti-inflammatory peptides under tolerizing conditions, or at least one pro-inflammatory peptide under immunizing conditions and at least one anti-inflammatory peptide under tolerizing conditions. Such a method of augmenting or inducing the inflammatory response results in an increase in the level of a pro-inflammatory cytokine such as interferon gamma (IFN.gamma.), tumor necrosis factor-alpha (TNF.alpha.), interleukin-1 (IL-1), IL-6, IL-12, or IL-23, in the subject, or a decrease in the level of an anti-inflammatory cytokine such as IL-4, IL-10, or transforming growth factor-beta (TGF.beta.), in the subject, or combinations thereof.
> [0010] In another embodiment, a method of the invention provides a means for reducing or inhibiting an inflammatory response in the subject. In one aspect, the method of reducing or inhibiting the inflammatory response is performed by administering a peptide having anti-inflammatory activity to the subject under immunizing conditions. In another aspect, the method is performed by administering a pro-inflammatory peptide to the subject under tolerizing conditions. In still another aspect, a combination of immunogenic peptides are administered, for example, two or more pro-inflammatory peptides under tolerizing conditions, or two or more anti-inflammatory peptides under immunizing conditions, or at least one pro-inflammatory peptides under tolerizing conditions and at least one anti-inflammatory peptide under immunizing conditions. Such a method of reducing or inhibiting the inflammatory response results in an increase in the level of an anti-inflammatory cytokine such as IL-4, IL-10, or TGF.beta.in the subject, or a decrease in the level of a pro-inflammatory cytokine such as IFN.gamma., TNF.alpha., IL-1, IL-6, IL-12, or IL-23, in the subject, or combinations thereof.
> [0076] As disclosed herein, one or a combination of immunogenic peptide portions of a dnaJ hsp can be administered, including, for example, any one or any combination of the immunogenic peptides exemplified by SEQ ID NOS:1-26. The skilled clinician will recognize in view of the present disclosure that a peptide of the invention is administered to a subject under immunizing conditions or under tolerizing conditions, depending on whether the peptide is a pro-inflammatory peptide or an anti-inflammatory peptide, and whether the peptide is being administered to augment or induce an inflammatory response or to reduce or inhibit an inflammatory response.

Note that none of these paragraphs appears to clearly teach that, for example, both pro- and anti-inflammatory peptides are to be co-administered, nor to they appear to teach that a pro-inflammatory peptide is to be administered with an anti-inflammatory cytokine. Note that "immunizing" and "tolerizing" conditions are disclosed in paragraph 77, provided below.

> [0077] As used herein, the term "under immunizing conditions" means that a peptide of the invention is contacted with a cell or administered to a subject such that it can effect its immunogenic activity. As such, the peptide, which is a T cell immunogen, generally will be administered in an immunogenic amount, typically as a priming dose followed some time later by one or more booster doses, intradermally, subcutaneously, or intramuscularly, and, if desired, formulated in a composition that includes an immunoadjuvant such as Freund's complete or incomplete adjuvant. As used herein, the term "under tolerizing conditions" means that a peptide of the invention is contacted with a cell or administered to a subject such that it induces tolerization to the otherwise immunogenic activity. As a result, a subject, for example, is tolerized to the peptide such that it is recognized a "self" by the subject and cannot effect an immune response. A peptide can be administered under tolerizing conditions by administering a tolerizing amount of the peptide, generally a small amount over a period of time, intradermally, subcutaneously, intramuscularly, or, preferably, mucosally, for example, via nasal spray or by eating.

Note that neither "immunizing" nor "tolerizing" conditions are taught as being brought about by the administration of cytokines. Further note the teachings of paragraph 63 of the specification (emphasis added by the examiner):

> [0073] The present invention also provide a composition, which contains at least one peptide of the invention and can provide a plurality of different immunogenic peptides of the invention, for example, a composition containing any of the peptides set forth as SEQ ID NOS:1-26, or a composition containing any combination of such peptides, particularly a composition containing a combination of pro-inflammatory peptides, and a composition containing a combination of anti-inflammatory peptides. A composition of the invention generally is formulated in a physiologically acceptable solution and, if desired, can further contain one or more immunoadjuvants, for example, one or more cytokines, Freund's complete adjuvant, Freund's incomplete adjuvant, alum, or the like. **Generally, where the composition contains one or more cytokines, the cytokines have an activity that is the same as or complements the inflammatory activity of the peptide of the invention.** The composition also can contain any immunoadjuvant, including an immunostimulant or, if desired, an immunosuppressant, which can modulate the systemic immune response of an individual. Suitable substances having this activity are well known in the art and include IL-6, which can stimulate suppressor or cytotoxic T cells, and cyclosporin A and anti-CD4 antibodies, which can suppress the immune response. Such compounds can be administered separately or as a mixture with a vaccine of the invention.

Therefore, it appears that the specification teaches that the cytokine administered with a peptide should complement, i.e. not have an activity that completely opposite, the activity of the administered peptide.

For the above reasons the rejection is maintained.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 64 and 65 also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed September 27, 2006 have been fully considered but they are not persuasive. Applicant argues that their arguments have overcome the rejection of record under 35 USC 101, and as such the rejection of claims 64 and 65 under 35 USC 112 should be withdrawn as well.

This argument is not persuasive because the rejection under 35 USC 101 has not been overcome as is discussed above. Therefore the rejection is maintained.

7. Claim 58 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the reasons of record.
The office action mailed June 28, 2006 states:

> Claim 58 recites a chimeric polypeptide wherein a peptide of recited SEQ ID number is linked to a heterologous polypeptide. The specification teaches chimeric polypeptides wherein peptides disclosed by SEQ ID number are *operatively linked* to heterologous polypeptides such that the functions of the individual elements comprising the fusion polypeptide are maintained (see particularly paragraph 56 on page 21 of the specification). As such the phrase operatively linked has been defined by the specification to have a specific meaning. A chimeric polypeptide comprising linked sequences is broader in scope than a chimeric polypeptide comprising operatively linked sequences, and the specification does not disclose chimeric polypeptides comprising linked sequences. Claim 58 as originally filed recited operatively linked chimeric polypeptides. Applicant's amendment to the claim to delete the word "operatively" broadens the claimed invention, and this broadening is new matter.

Applicant's arguments filed September 27, 2006 have been fully considered but they are not persuasive. Applicant argues that "deletion of the term 'operatively' does not expand the scope of the originally filed claim since each of the peptides must necessarily have the activity disclosed in the specification."

This argument is not persuasive. The specification teaches:

> An immunogenic peptide of the invention also can be modified by being operatively linked to one or more other peptides or polypeptides. As such, the present invention also provides a chimeric polypeptide, which includes a peptide of the invention operatively linked to at least one heterologous polypeptide. As used herein, the term "operatively linked" means that two or more peptides (or two or more polynucleotides) are joined together such that the functions of the linked peptides (or polynucleotides) is maintained, and such that the chimeric polypeptide (or recombinant nucleic acid molecule) exhibits the functions of each component peptide (or polynucleotide). For example, a chimeric polypeptide of the invention can include a

> peptide of the invention operatively linked to a peptide tag such as a polyhistidine tag, such that the peptide can be identified in a sample or isolated from a mixture using a nickel chelate reagent.

As such, the functional activities that comprise an "operatively" linked peptide are clearly defined. Applicant's arguments that "operatively linked peptides" and "linked peptides" are equivalent because the word operatively is "merely descriptive" is not convincing since applicant does not point to where the specification it is disclose that the terms are synonymous. Further, it is known in the art that fusion constructs comprising sequences from two distinct sources can yield a construct that does not comprise the activities present in the staring non-fused sequences (Link et al., see entire document, particularly the abstract). As such, in the absence of an explicit teaching that either "operatively linked" and "linked" peptides are synonymous or disclosure of a separate definition specific for "linked peptides" a skilled artisan would not reasonably assume that the two terms were synonymous and that "linked polypeptides" necessarily comprised the same activities as the starting materials. Therefore the rejection is maintained.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 58 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record.

The office action mailed June 28, 2006 states:

> Claim 58 recites a chimeric polypeptide wherein a peptide of recited SEQ ID number is linked to a heterologous polypeptide. The specification teaches chimeric polypeptides wherein peptides disclosed by SEQ ID number are *operatively linked* to heterologous polypeptides such that the functions of the individual elements comprising the fusion polypeptide are maintained (see particularly paragraph 56 on page 21 of the specification). As such the phrase operatively linked has been defined by the specification to have a specific meaning. A chimeric polypeptide comprising linked sequences is broader in scope than a chimeric polypeptide comprising operatively linked sequences, but the specification does not teach the metes and bounds of linked sequences. Specifically, do the functions of the individual elements that comprise a linked polypeptide need to be maintained as they are in an operatively linked chimeric polypeptide, or are other functional properties required of chimeric polypeptides comprising linked polypeptides? If the later, what are these properties?

Applicant's arguments filed September 27, 2006 have been fully considered but they are not persuasive. Applicant argues that "deletion of the term 'operatively' from the claim does not render the claim indefinite since "the two peptides are linked such that the functions of the linked peptides is [sic] maintained."

This argument is not convincing because the specification defines "operatively linked peptides" and maintaining function but does not define "linked peptides" in this manner and because a skilled artisan would know that when peptides are linked functions of the individual peptides are not necessarily maintained as is demonstrated by the teachings of Link et al. (see entire document, particularly the abstract). As such the claim is indefinite.

10. Claims 57, 59, 62, 63, and 66 are allowable.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
November 21, 2006

12/2/06
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER